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Conclusions are not warranted from this limited experience. It must be borne in mind that we are dealing with a disease with apparent tendency to recurrence. Frequently it appears to clear up under divers conditions, so that the term "recovery" must, until we know better, refer to the immediate condition under observation. Similarly the use of solid food in every case of pellagra may be inadvisable or impracticable; for instance, when very severe stomatitis is present. The unusually favorable experience with the severe cases herein reported on would, however, suggest the inference that diarrhea in itself is no contraindication to the use of solid food, even in large amounts, that a generous diet seems to have a decidedly favorable effect upon the course of pellagra, confirming an observation that had been made even before Strambio's time. It is evident that the arsenicals at present so much in vogue may be dispensed with without harm, if not actual benefit to the patient.

THE CEREBROSPINAL FLUID IN PELLAGRA.

By W. F. LORENZ, Special Expert, United States Public Health Service, and Director Wisconsin Psychiatric Institute.

While pellagra has been very diligently investigated, relatively little attention has been directed toward the cerebrospinal fluid. The few contradictory reports that have appeared in this connection suggested the advisability of further investigation in this particular field.

In 1912 Boveri (1) reported a series of examinations and concluded that a slight lymphocytosis and an excess of globulin were present in the spinal fluid. Hindman (2) made a somewhat similar report in the same year. Buhlig and Holmes (3) made a contradictory report from three cases, and Dudgeon (4) also found a negative fluid in the two fatal cases of pellagra reported from England. In a later report Hindman (5) attributes some of his former finding to syphilis, and claims that after his cases of pellagra were controlled by Wassermann examinations practically none showed a lymphocytosis.

The data contained in this report were obtained from 153 spinal fluid examinations made in 106 cases of pellagra. Practically every clinical type of pellagra is represented in this series. Very acute cases, with severe mental and physical manifestations, contribute the largest share. On some of these a second puncture was made after the acute condition had subsided. In a number of cases a third confirmatory examination was made after an interval of several months. This series also includes a number of cases that showed very little or no mental disturbance.

The routine examination consisted of a cell count, an estimation of the globulin constituent, and a Wassermann (Noguchi) and Lange's colloidal gold chloride test.

The cell count was made as follows: Immediately after lumbar puncture the fluid was drawn into a red cell mixing pipette which had been previously prepared by drawing a very small amount of stain into its chamber. This stain consists of a 2 per cent glacial acetic acid solution colored with gentian violet, allowing a few minutes for the cells to stain; the pipette was thoroughly shaken in order to get an even distribution of the cells in the fluid. The first few drops are discarded. In this work the Turek counting chamber was used, and as a routine two counts were made. All nucleated elements were counted as lymphocytes. Of the 106 cases examined, 96 gave a count of less than 5 cells per cubic millimeter. In 2 cases the cell count ranged from 6 to 9 cells per cubic millimeter, while in 8 cases the count indicated a lymphocytosis ranging from 20 to 60 cells per cubic millimeter.

The 8 cases that gave a lymphocytosis were positive to the Wassermann with both spinal fluid and blood serum; all the globulin tests were also positive, and the colloidal gold chloride test gave a curve typical for paresis. In 6 of these 8 cases a positive history of luetic infection was obtained. As a consequence these 8 cases are regarded as pellagrins complicated with syphilis, and the spinal fluid findings in them are attributed to the syphilitic infection.

For the detection of a pathological excess of globulin the Noguchi butyric acid test and Ross-Jones modification of the Nonne-Appelt test were used. The results of these tests paralleled one another fairly well. From previous experience it is concluded that these tests gave essentially identical results, so that their combined results will be summarized as one test. As previously mentioned, the 8 cases of combined pellagra and syphilis were positive to these tests. In addition, 7 cases of uncomplicated pellagra gave fairly positive reactions and 18 gave reactions that were designated as "weakly positive." Of the 7 cases that gave positive results, 6 were extremely emaciated, almost moribund cases. These results are partially confirmatory of the globulin excess found by others, yet not to the same extent, there being but 25 cases of the 106 that showed positive and weakly positive reactions. In the reading of either the Noguchi butyric acid test or of the Ross-Jones very slight departure from the reaction of normal fluid was noted and designated as "weakly positive." If the frankly positive cases alone are considered, the occurrence of an excess of globulin would be in less than 8 per cent.

For the Wassermann examination made in these cases I am indebted to Dr. S. S. Hindman, pathologist at the Georgia State Sani-

tarium, Milledgeville, Ga. The human or Noguchi hemolytic system was employed, and in every case two antigens were used. One was an alcoholic extract of luetic liver and the other cholesterin fortified antigen made by adding 0.4 per cent cholesterin to an antigen made from guinea-pig heart, according to the Noguchi method. In all but a few cases both the blood serum and spinal fluid were tested.

The results from the Wassermann tests were uniformly negative, with the exception of the 8 cases of syphilis and 2 cases in which no history or other evidence of syphilis could be obtained. Both of these patients were severely ill; the blood serum alone gave weakly positive reactions. The spinal fluid did not inhibit hemolysis. In both cases the specimens of blood and spinal fluid were taken a few days before death.

The Lange colloidal gold chloride test was applied in the following manner: In the first of 10 test tubes 0.2 c. c. of spinal fluid was mixed with 1.8 c. c. freshly prepared 0.4 per cent sodium chloride solution; 1 c. c. of this mixture was diluted with 1 c. c. of the sodium chloride solution in tube No. 2, thus securing a half dilution of the 1 to 10 dilutions in tube No. 1. These succeeding half dilutions were made throughout the series of 10 test tubes; 5 c. c. of the colloidal gold chloride solution were then added to each tube and the rack was set aside for 24 hours at room temperature, when a reading was made. Excepting the 8 cases of syphilis, none gave any reaction with the "gold sol." In a few cases very slight color changes were noted in the lower dilutions, though hardly sufficient to be designated as 1+.

Pressure estimations of the spinal fluid are, in my opinion, of very doubtful value. Very high tension is frequently found in the various meningitides. In such instances an apparatus to measure this pressure is not needed. Its forceful expulsion is sufficient to indicate the high tension that exists. Using a capillary tube attached to the lumbar puncture needle, a large number of cases were observed, and the conclusion reached was that changes in fluid tension up to 100 mm. of fluid height could be brought about by the slightest muscular effort on the part of the patient. Such efforts as coughing, deep breathing, etc., would cause great alteration in the fluid tension. As a consequence, little significance is attached to the variations of tension within 50 or 100 mm. That beneficial effects in the delirium so frequently observed in severe cases of pellagra occurred after the withdrawal of 20 to 30 c. c. of fluid is undoubted. In these cases, however, the fluid was not necessarily under greater tension than in the nondelirious cases. As a rule, the feeble, apathetic cases with poor circulation showed a reduction in the fluid tension, so much so that in some instances it took several minutes to obtain 4 or 5 c. c.

As a result of this investigation it is concluded that a lymphocytosis does not occur in an uncomplicated case of pellagra. This finding is quite in accord with the recent reports of the histo-pathology of the nervous system in this disease. Mott (6) could find no evidence of meningeal or perivascular infiltration with lymphocytes, plasma cells, or polynuclear leucocytes. Likewise Singer and Pollock (7) failed to find any condition that would occasion a lymphocytosis of the cerebrospinal fluid.

The negative fluid in pellagra can be taken into consideration when the question of etiology is considered. The well-known diseases of the central nervous system due to bacterial invasion are almost invariably accompanied by a pathological spinal fluid. The same is true when the central nervous system is infected by the spirochaeta or the trypanosome. The absence of any evidence in the form of a lymphocytosis or an increase of any of the nucleated elements of the spinal fluid points to the absence of an infection with inflammatory lesions in close proximity to the circulating (cerebrospinal) fluid.

Summary and Conclusions.

Summarizing the results of this investigation, the following conclusions are offered:

1. A lymphocytosis of the cerebrospinal fluid does not occur in uncomplicated pellagra.
2. Globulin excess of the spinal fluid is only occasionally observed.
3. Lange's colloidal gold chloride test is uniformly negative in pellagra.
4. The Wassermann is negative with a few exceptions. In this investigation the exceptions were moribund cases which gave weakly positive reactions with blood serum.
5. The spinal-fluid findings would seem inconsistent with a conception that pellagra is an infectious disease of the central nervous system.

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References.

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